Effect of Bacillus Calmette-Guérin vaccination on the immunogenicity of the mRNA BNT162b2 COVID-19 vaccine in health care workers

Published: 21-01-2021
Last updated: 04-04-2024

To determine the impact of prior BCG vaccination on the duration of immunogenicity of the BioNTech/Pfizer mRNA COVID*19 vaccine.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON50881

Source
ToetsingOnline

Brief title
COMBI study

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
Corona, COVID-19

Research involving
Human

Sponsors and support

Primary sponsor: Interne Geneeskunde

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Adaptive immunity, BCG Vaccine, COVID-19, Vaccines

Outcome measures

Primary outcome

Serological titer of IgG to the SARS-CoV-2 spike protein at 6 and 12 months

after the Pfizer/BioNTech BNT162B2 vaccination.

Secondary outcome

- Geometric mean concentrations (GMCs) of RBD- and S-specific IgG, IgA and IgM

in serum at day 35 after the first dose of the Pfizer/BioNTech BNT162B2

vaccination;

- IgG, IgA and IgM concentrations against SARS-CoV-2 antigens in nasal mucosal

lining fluid at the various sampling time points.

- Local reactions at injection site or systemic reactions after COVID-19

vaccination.

- T-cell responses and monocyte cytokine response to ex vivo stimulation at the

various time points.

Study description

Background summary

At the time of writing, more than 85 million have been infected by the virus and more than 1,8 million died in association with the virus. Next to the global health, the coronavirus had a great impact on people*s daily life and the global economy.

As of January 2021, the Netherlands is confronted with a second wave and the

country went back into lockdown. However, in the last weeks of 2020 there has been the long-awaited news that Covid vaccines of several companies, among which Pfizer, show about 95% efficiency. The vaccine has also been approved by the EMA at 21 December 2020 and the Dutch vaccination program started January 8. Employees working in the COVID-19 frontline belong to the first group who will get offered the vaccine.

In the course of the pandemic, it was unforeseeable when a Covid vaccine would come available, thus researchers worldwide were searching for alternative preventive measures. It has been shown for several years that the Bacillus Calmette-Guérin (BCG) vaccination, a vaccine originally made against tuberculosis, develops immunological memory in innate immune cells, a process termed trained immunity. In addition, recent studies have suggested that COVID* 19 incidence and mortality rate are lower in countries where the BCG vaccine is a part of the routine childhood immunisation schedule. Therefore, several trials with different study populations have been set up to investigate whether BCG can indeed protect against COVID-19. The first (interim) analyses will be conducted within the next weeks.

Next to the unspecific protective effects of BCG, it is hypothesized that BCG vaccination can enhance the immunogenicity of other vaccines. This has been proven for the influenza and pertussis vaccines. BCG vaccination prior to influenza or pertussis vaccinations results in a more pronounced increase and accelerated induction of functional antibody responses. Our aim is to investigate whether prior BCG vaccination can also enhance the immunogenicity of the COVID*19 mRNA vaccine developed by BioNTech and Pfizer. By enhancing antibody response through prior BCG vaccination, protection against COVID-19 may last longer after vaccination with the COVID-19 vaccine.

Study objective

To determine the impact of prior BCG vaccination on the duration of immunogenicity of the BioNTech/Pfizer mRNA COVID*19 vaccine.

Study design

A single center open label intervention study.

Intervention

One group has been vaccinated with BCG in the past 12 months and will be vaccinated with the COVID-19 vaccine from Pfizer/BioNTech. The other group has never been vaccinated with BCG and will be vaccinated with the COVID-19 vaccine from Pfizer/BioNTech.

Study burden and risks

In this study, patients will be asked to undergo a venipuncture and nasal mucosal lining fluid sampling which are measurements of invasive nature. Venipuncture may be painful and may cause hematoma. Obtaining mucosal lining fluid by nasosorption may be experienced by participants as 'tickling' and induce sneezing and/or tearing. However, sampling will be done by experienced researchers and does not form any risk to the health of the subject.
Positive results from this study could lead to an increased efficacy of COVID-19 vaccines and thereby help to combat the pandemic.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age equal to or above 18 years;
- Written informed consent provided by the participant;

- Receiving BioNTech/Pfizer COVID-19 vaccine per routine care;
- Having received BCG-vaccination in the past 12 months OR never having received BCG-vaccination.

Exclusion criteria

- Legally incapacitated or unwilling to provide informed consent;
- History of COVID-19 infection, confirmed by a microbiological test.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-04-2021
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BNT162b2 COVID-19 vaccine

Ethics review

Approved WMO Date:	21-01-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	25-03-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-000182-33-NL
CCMO	NL76421.091.21